

IN THE SPECIFICATION

Please delete the Sequence Listing filed August 21, 1998, and insert therefor the attached paper copy of the Substitute Sequence Listing after page 57, between the specification and the claims.

Please delete page 9, 5th full paragraph, line 25 - page 10, line 2, and insert therefor the following paragraph:

In one embodiment, the objects of the invention are achieved by providing an antibody or fragment thereof that activates a hematopoietic growth factor superfamily receptor having a biological activity with 2 orders of magnitude (100), preferably within one order of magnitude (10), of the natural ligand on a weight basis. Preferably, the antibody activates the thrombopoietin (TPO) receptor. This antibody, referred to as an agonist antibody, activates a thrombopoietin receptor which preferably comprises a mammalian c-mpl, more preferably human c-mpl. Usually the antibody will be a full length antibody such as an IgG antibody. Suitable representative fragment agonist antibodies include Fv, ScFv, Fab, F(ab')₂ fragments, as well as diabodies and linear antibodies. These fragments may be fused to other sequences including, for example, the F'' or Fc region of an antibody, a "leucine zipper" or other sequences including pegylated sequences or Fc mutants used to improve or modulate half-life. Normally the antibody is a human antibody and may be a non-naturally occurring antibody, including affinity matured antibodies. Representative antibodies that activate c-mpl are selected from the group 12E10 (SEQ ID NO: 77), 12B5 (SEQ ID NO: 75), 10F6 (SEQ ID NO: 72) and 12D5 (SEQ ID NO: 76), and affinity matured derivatives thereof. Other preferred agonist antibodies to c-mpl are selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5 and Ab6, wherein each Ab1-Ab6 contains a VH and VL chain and each VH and VL chain contains complementarity determining region (CDR) amino acid sequences designated CDR1, CDR2

and CDR3 separated by framework amino acid sequences, the amino acid sequence of each CDR in each VH and VL chain of Ab1-Ab6 is shown in Table 1.

Please delete page 11, 4th full paragraph, lines 10-11, after “Brief Description Of The Drawings”, and insert therefor the following paragraph:

Fig. 1 shows examples of single chain antibody (scFv) fragments denominated 10F6 (SEQ ID NO: 72), 5E5 (SEQ ID NO: 73), 10D10 (SEQ ID NO: 74), 12B5 (SEQ ID NO: 75), 12D5 (SEQ ID NO: 76) and 12E10 (SEQ ID NO: 77) having sequences for CDRs and framework regions.

Please delete page 23, 3rd paragraph, lines 12-15, and insert therefor the following paragraph:

Preferred scFv fragments denominated 10F6 (SEQ ID NO: 72), 5E5 (SEQ ID NO: 73), 10D10 (SEQ ID NO: 74), 12B5 (SEQ ID NO: 75), 12D5 (SEQ ID NO: 76) and 12E10 (SEQ ID NO: 77) having sequences for CDRs and Framework regions provided in Figure 1. Alternatively, the above enumerated scFvs are affinity matured by mutating 1-3 amino acids residues in one or more of the CDRs or in the framework regions between the CDRs.